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Fundus Camera as a Screening for Diabetic Retinopathy in AMC Yogyakarta Indonesia

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Abstract
Backgrounds: Diabetes mellitus is a global burden disease. Indonesia ranks the seventh highest in the world with the number of patients reaching 8.5 million people. The highest prevalence of diabetes is in Yogyakarta. Diabetic retinopathy is the most common micro vascular complication, which is a leading cause of preventable blindness in working-aged people. Fundus Camera is used to capture images of the interior surface of the eye. It can be used to screening for diabetic retinopathy.**Objective:** To evaluate diabetic retinopathy screening using fundus camera in AMC Yogyakarta and its risk factors such as poor glicemic control, hypertension, and smoking **Methods:** Cross sectional study, the number of sample was 45 patients suffering from diabetes mellitus during the period 2012-2014. Statistical test was Chi Square Test.**Results:** Significant correlation between duration of diabetes mellitus probability risk factor to develop diabetic retinopathy OR 0,215 95% CI: (0,087 to 0,529) (p 0.001), controlled blood glucose probability risk factor to increase severity of diabetic retinopathy OR 27 95% CI:(1,26 to 578) (p 0,041), and duration of diabetes mellitus probability risk factor that make severity of diabetic retinopathy worse (p 0,044). The others analysis result is not significant.**Conclusion:** Diabetic retinopathy was significantly correlated with a duration of diabetes mellitus, and severity of diabetic retinopathy was significantly correlated with controlled blood glucose and duration of diabetes mellitus.
Keywords: diabetic retinopathy, fundus camera, diabetes mellitus

Introduction

Diabetes mellitus is a global burden disease. The majority of 382 million people with diabetes were between 40 and 59 years old, and 80% of whom lived in low- and middle-income countries. The number of people with diabetes will increase by 55% by 2035. The burden of diabetes is enormous, both in human and finance provoking 5.1 million deaths and taking up some USD 548 billion dollars in health spending (11% of the total spent worldwide) in 2013. Indonesia ranks the seventh highest in the world with the number of patients reaching 8.5 million people[1]. The highest prevalence of diabetes is in Yogyakarta[2].

Diabetes mellitus is a long-term disease which if uncontrolled may lead to complications in some organs. In general, the long-term complications of diabetes can be divided into micro vascular and macro vascular complications. Micro vascular complications involve small blood vessels while makrovascular complications involve medium and large blood vessels. Micro vascular complications include diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy, meanwhile macrovascular complications include atherosclerosis, stroke, and gangrene of extremities due to diabetes mellitus[3]. The most common micro vascular complication of diabetes mellitus is diabetic retinopathy, which is a leading cause of preventable blindness in working-aged people. It has been estimated that diabetic individuals are 25 times more likely than their nondiabetic counterparts to suffer severe, permanent vision loss, although the pathogenesis of diabetic retinopathy is still not fully understood[4].

The prevalence of all types of diabetic retinopathy in the diabetic population increases with the duration of diabetes mellitus and patient age. Diabetic retinopathy is rare in children younger than 10 years old. The risk of developing diabetic retinopathy increases after puberty. The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), an ongoing epidemiologic study on the progression of diabetic retinopathy, involved assessments using 7-field stereoscopic fundus photography, measurements of glycosylated hemoglobin levels, and recording of visual acuity. The WESDR reported important epidemiologic findings, including the duration of diabetes mellitus which was directly associated with an increased prevalence of diabetic retinopathy. After 20 years of diabetes mellitus, nearly 60% with type 2 had some degree of diabetic retinopathy, and 1.6% of older-onset patients (aged ~30 years at diagnosis, an operational definition of type 2 diabetes mellitus) were found to be legally blind. Diabetic retinopathy caused legal blindness in 86 % and 33% for the younger-onset and older-onset groups respectively[5].

Clinically, diabetic retinopathy divided to Non-Proliferative Diabetic Retinopathy (NPDR) and Proliverative Diabetic Retinopathy (PDR). NPDR will continue to PDR, which would there is a neovascularization formation. The neovascularization is fragile and can cause bleeding[6].

The presence of diabetic retinopathy is an indicator for increasing morbidity and mortality (including cardiovascular complications). Patients with proliferative retinopathy and non-proliferative retinopathy compared with patients without retinopathy are facing with a high risk of cardiovascular events, including

Myokard Infark, Stroke, Revascularization, and death from Coronary Vascular Desease[7]. Screening for diabetic retinopathy is important, because the large number of patients had no symptoms with progression of diabetic retinopathy to the clinically significant macular edema (CSME) and PDR. On the other hand, the effect of laser photocoagulation in preventing vision loss from PDR and CSME has been marked in the randomized trials. Early prevention of retinopathy is more important than the treatment of established diabetic retinopathy[8].

Fundus Camera is used to capture images of the posterior surface of the eye. These images of the retina, optic disc, macula and posterior pole are digital, which enables quick transfer and detailed image study as well as side-by-side image comparison and longitudinal tracking over time. Retinal imaging presents a unique difficulty considering that the retina must be illuminated and imaged simultaneously, a process which forces illumination and imaging systems to share a common optical path. Because the retina is a minimally reflective surface, the power of the back reflections from the shared optics of the illumination and imaging paths is greater than the power reflected by the retina. These images are the key in the identification and care of various eye diseases[9].

The objective of this study was to evaluate for diabetic retinopathy screening in diabetic mellitus patient using fundus camera in AMC Yogyakarta and its risk factors such as controlled blood sugar, hypertension, and smoking.

Methods

This research was an analytical observational study using a retrospective cross-sectional approach which aimed to know the risk factor of diabetic retinopathy. The data were collected from medical records of AMC Eye Center between January 2012 and December 2014. The primary data were collected from questionare and the secondary data were collected from medical records of AMC. Fourty-five sample and data were analyzed using Chi-Square test and POR was calculated with same formula as OR[10]. All tests were two tailed, p-values <0.05 were accepted as statistical significance[11].

Results

The results can be shown bellow

Table 1. Frequences of diabetic retinopathy by age

Usia	Frequency	Presentase (%)
31-41	2	4,4
41-50	10	22,2
51-60	23	51,2
61-70	7	15,5
>70	3	6,7

Diagram 1 present the percentage of diabetic retinopathy based on age. 4,4% was in 31-40 years old, 22,2% was in 41-50 years old, 15,5% was in 61-70% years old, and 6,7% was over 70 years old. The highest prevalence was in group 51-60 years old.

Table 2. Percentage of diabetic retinopathy by sex

Sex	Frequency	Percentage (%)
Man	17	38%
Woman	28	62%

Table 2 show that diabetic retinopathy cases in AMC Yogyakarta, from 2012 until 2014 were higher in women than in men with 62% and 38%.

The observation of the images from the fundus camera then processed with data which is obtained from the questionare, showed in the following tables.

Table 3. Analysis result between duration of diabetes and diabetic retinopathy

		Diabetic Retinopathy					
		Yes	No	*P*	OR	CI	
		%	%			Lower	Upper
Duration of Diabetes	< 5 years	15,6%	26,6%	0,001	0,215	0,087	0,529
	> 5years	42,2%	15,6%				
Total		57,8%	42,2%				

Table 3 shows the amount of people who suffered diabetes mellitus less than 5 years who gets diabetic retinopathy were 15,6% and people who suffered diabetes mellitus over 5 years who gets diabetic retinopathy were 42,2%. From the analysis, p 0,001 with OR 0,215 (95% CI:(0,087-0,529)).

Table 4. Analysis result between duration of diabetes and severity of diabetic retinopathy

		Diabetic Retinopathy					
		NPDR	PDR	*P*	OR	CI	
		%	%			Lower	Upper
Duration of Diabetes	< 5 years	12,3%	3,3%	0,044	4,074	0,978	16,967
	> 5years	20%	22,2%				
Total		32,3%	25,5%				

On the table above, it can be seen that 32,2% get NPDR and 25,5% get PDR. This amount is diveded into 2 groups which consist of 12,3% of NPDR is people who suffered diabetes mellitus less than 5 years, and 20% of NPDR is people who suffered diabetes mellitus over 5 years. In poliferatif diabetic retinopathy stage, 3,3% was people who suffered diabetes mellitus less than 5 years, and 22,2% was people who suffered diabetes mellitus over 5 years. From the analysis, p 0,44 with OR 4;074 (95% CI:(0,978-16,967)).

Table 5. Analysis result between controlled blood glucose and severity of diabetic retinopathy

		Diabetic Retinopathy					
		NPDR	PDR	*P*	OR	CI	
		%	%			Lower	Upper
Glicemic control	Intensive	56,25%	6,25%	0,041	27	1,26	578
	Poor	6,25%	18,75				
Total		62,45%	25%				

From all of patient with intensive glicemic control shows that 56,25% was diabetic retinopathy in NPDR stage and 6,25% was in PDR stage. In the other hand, in patient with poor glicemic control show that the amount of patient with PDR was more than NPDR with total 18,75% and 6,25%. From the analysis, p 0,041 with OR 27 (95% CI:(1,26-578)).

Table 6. Analysis result between hypertension and severity of diabetic retinopathy

		Diabetic Retinopathy					
		NPDR	PDR	*P*	OR	CI	
		%	%			Lower	Upper
Hipertension	Yes	12,5%	12,5%	0,52	0,25	0,21	3,041
	No	8,9%	12,5%				
Total		21,4%	25%				

From the table, the amount of people with hypertension who gets diabetic retinopathy in NPDR stage and PDR stage were the same, which were 12,5%. However the amount of non hypertension people who gets diabetic retinopathy in NPDR stage and PDR stage were 8,9% and 12,5%. From the analysis, p 0,52 with OR 0,25 (95% CI:(0,21-3,041)).

Table 7. Analysis result between smoking and severity of diabetic retinopathy

		Diabetic Retinopathy					
		NPDR	PDR	*P*	OR	CI	
		%	%			Lower	Upper
Smoking	Yes	12,5%	12,5%	0,52	0,25	0,21	3,041
	No	8,9%	12,5%				
Total		21,4%	25%				

The result from the table above is same with the previous table. the amount of smoker who gets diabetic retinopathy in NPDR stage and PDR stage were the same, which were 12,5%. However the amount of non smoker people who gets diabetic retinopathy in NPDR stage and PDR stage were 8,9% and 12,5%. From the analysis, p 0,52 with OR 0,25 (95% CI:(0,21-3,041)).

Table 8. Analysis result between duration of diabetes and CSME

		CSME					
		Yes	No	*P*	OR	CI	
		%	%			Lower	Upper
Duration of diabetes	< 5 years	4,4%	37,8 %	0,36	0,56	0,159	1,98
	> 5 years	10%	47,8%				
Total		14,4%	85,6%				

From the table above, 4,4% people who suffered diabetes mellitus less than 5 years and 10% people who suffered diabetes mellitus over 5 years suffer of CSME. From the analysis, p 0,36 with OR 0,56 (95% CI: (0,159-1,98)).

Discussion

From the table 1, the highest prevalence was in group 51-60 years old. Based on epidemiological studies, patients with retinopathy had the highest distribution in the age range 20-60 years old[12]. Ninety percent of patients with diabetes mellitus is diabetes mellitus type 2, which often occurs at the age of 30 years old and it is increasing at age over 45 years old as the start of the degeneration of the body's cells physiologically[13].

On the table 2, female patient was more than male. There has not been any study about the correlation between retinopathy and sex. However, it has been reported that estrogen hormones induces diabetes mellitus, where women with DM have higher risk of diabetic retinopathy than men do. This high number of diabetic retinopathy is related to the high number of fat in women. High rate of diabetic retinopathy in woman is associated with high rate of obesity caused by genetic and lifestyles, which are the risk factors of diabetes mellitus. Estrogen is the most dominant hormon in women. High estrogen level may reduce leptin, which has an important role of apetite in hypotalamus, so the food intake becomes uncontrolled. It may trigger the accumulation of excess lipid tissues and higher level of blood sugar due to the reduction of peripheral tissues sensitivity to insulin[14].

On the table 3, analysis result between the duration of diabetes mellitus and diabetic retinopathy from 45 samples of diabetic retinopathy patients shows that there was a significant correlation between duration of diabetes mellitus and diabetic retinopathy (p=0,001). Individu with the shorter duration of diabetes mellitus has 0,215 higher risk than the longer duration (OR= 0,215 (95% CI:(0,087-0,529)). In accordance with previous studies, duration of diabetes was significantly correlated with any diabetic retinopathy and increased grade of diabetic retinopathy. In our study, the frequency of any diabetic retinopathy increased when the duration of diabetes was more than 5 years. This was similar to the findings in the other Nordic studies[15].

On the table 4, the data analysis for the association between duration of diabetes and diabetic retinopathy on NPDR and PDR stage shows a significant result, because p value was 0,044 which was less than 0,05 but the result of OR is unnecessary. So, the analysis result supports the hypothesis about the difference severity from diabetic patients by their duration of diabetes. This was similar to the findings from Heinrich-Cybulska, et al (2015) that mentioned duration of diabetes is the main risk factor for both the incidence of NPDR and the conversion to PDR[16].

The next table, table 5 which is the result of data analysis the relationship between blood sugar control with diabetic retinopathy on NPDR and PDR stage. Because the expected value was less than 5, so the analysis used *Fisher exact test*. The result was significant, p 0,041 which was less than 0,05 so there was an acossiation between intensive glicemic control and diabetic retinopathy severity. The result of OR is 27 (95% CI:(1,26-578)) which means people with poor glicemic control has risk 27 times to get diabetic retinopathy than people with intensive glicemic control. Diabetes Control and Complications Trials (DCCT) and United Kingdom Prospective Diabetes Study demonstranted that intensive glycemic control is associated with a reduced risk of newly diagnosed retinopathy and reduced progression of existing retinopathy in people with diabetes mellitus. According to the DCCT, intensive insulin therapy reduced the incidence of new cases of diabetic retinopathy by as much as 76% compared with conventional therapy[17].

On the table 6, the analysis result between hypertension and diabetic retinopathy can be showed that p was more than 0,05, that means there was no association between hypertension and diabetic retinopathy. The result of OR is unnecessary. This is same as the research from Hu, et al (2012) which said that blood pressure control within the normal range had no effect on preventing diabetic retinopathy progression[18]. But this result is different with the research from Yau, et al (2012) that confirmed the importance and impact of major modifiable risk factors such as hypertension on the risk of all diabetic retinopathy end points, including for the first time, PDR and CSME[19]. Hypertension is more common in diabetes mellitus than in the general population. In people who suffered diabetes mellitus, it was thought to reflect concurrence of two common conditions. Recent observations concerning interrelationships among glucose, insulin, body mass, fat metabolism, sodium homeostasis, renal function and the systemic vasculature in blood pressure regulation offer new insights into the mechanisms underlying high blood pressure in DM.

Almost all studies evaluating total body exchangeable sodium in diabetic patients have found increased sodium content, 10% higher than in nondiabetic subjects. The increase in exchangeable sodium is explained partially by active reabsorption of glucose and ketones in the kidney as sodium salts[20]. The differences in results of this study might be due to the subject of our studies had have controlled their blood pressure. Nevertheless, the results should be investigated in a larger study population.

The result of table 7 is same with table 6. From the analysis result between smoking and diabetic retinopathy can be obtained that p was more than 0,05, that means there was no association between smoking and diabetic retinopathy. The result of OR was unnecessary. Smoking seems to be related to the development of the diabetic retinopathy, but the evidence is not so clear. While EURODIAB IDDM Complications Study demonstrated that smoking is a risk factor for the development and progression of diabetic retinopathy[21]. Other studies showed that smoke is not a significant risk factor in this case. Research from Zhong, et al (2011) mentioned that smoking is related to diabetic retinopathy. Accordingly, smoking greatly increases the risk of endothelial dysfunction in microvaskular and macrovascular complication particularly in diabetic patients, manifesting substantially increased risk of complications such as diabetic retinopathy. Therefore, smoking control might prevent or reduce the risk of diabetic microvascular and macrovascular complications[22,23].

Beside to the incidence of diabetic retinopathy, macular edema also found in our study. Macular edema

is the most common etiology of visual loss due to diabetic retinopathy[24]. Macular edema can cause visual disturbances significantly. As known as the blind spot is the point where the vision fall in the retina, if there are abnormalities in the blind spot area, it will produce a situation where the eye can not see clearly. Depends on the severity of macular edema, 25%-30% of eyes with CSME will have moderate visual loss within 3 years[25]. Visual acuity should also be measured. Although it does not aid in the diagnosis of CSME initially, at least, patients may have a visual acuity of 20/20, it is an important parameter in following the progression of macular edema[26]. Table 12 showed that duration of diabetes mellitus is not a significant risk factor for macular edema, because like study from Mathew, et al (2015) that mentioned that considering that macular edema develops as a sequela of diabetes mellitus, we would expect an association between poor control of blood glucose levels and deterioration in macular edema[27].

Excluding to the analysis results, fundus camera has a weakness and less accurate than funduskopi. Nevertheless, fundus camera has the advantage of documenting pogresifitas diabetic retinopathy[28].

Conclusion

From the results can be summarized as follows

1. There is an association between the incidence of diabetic retinopathy with duration of diabetes mellitus, but has no effect to the severity of diabetic retinopathy.
2. Duration of diabetes mellitus no related to CSME.
3. Intensive blood control has a association with the severity of diabetic retinopathy.
4. The other risk like hypertension, and smoking has no association with diabetic retinopathy on the patient whom get treated in the AMC Yogyakarta.

Therefore, early screening of diabetic mellitus patients become a necessity in order to identify diabetic retinopathy and prevent the risk of blindness.

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